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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/444,067	11/19/1999	BRIAN R. MURPHY	17634-000512	8148

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EXAMINER

BRUMBACK, BRENDA G

ART UNIT PAPER NUMBER

1642

DATE MAILED: 03/04/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

# Office Action Summary

Application No.

09/444,067

Applicant(s)

MURPHY ET AL.

Examiner

Brenda G. Brumback

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

## Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

## Status

- 1) ☒ Responsive to communication(s) filed on 09 November 2001.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

## Disposition of Claims

- 4) ☒ Claim(s) 63-78, 88-122, 128-145 and 147-161 is/are pending in the application.
- 4a) Of the above claim(s) See Continuation Sheet is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 63-67, 89, 93-95, 120-122, 128-136, 148, 150, and 160 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

## Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on \_\_\_\_\_ is: a) ☐ approved b) ☐ disapproved by the Examiner.
- If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

## Priority under 35 U.S.C. §§ 119 and 120

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some \* c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- \* See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
- a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

## Attachment(s)

- 1) ☐ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) \_\_\_\_\_.
- 4) ☐ Interview Summary (PTO-413) Paper No(s). \_\_\_\_\_.
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: \_\_\_\_\_.

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### **DETAILED ACTION**

1. This action is responsive to the amendment filed 11/09/2001 and the subsequent communication filed 02/25/2002. Claim 120 was amended.

Claims 63-78, 88-122, 128-145, and 147-161 are pending.

Claims 68-78, 88, 90-92, 96-114, 115-119, 137-145, 147, 149, 151-159 and 161 have been withdrawn from consideration.

Claims 63-67, 89, 93-95, 120-122, 128-136, 148, 150, and 160 are under examination to the extent that they read on the elected species, recombinant RSV with an SH gene deletion.

#### ***Information Disclosure Statement***

2. The IDS filed 07/31/2000 (Paper # 7) has not yet been considered, as the parent file containing the references (U.S. Application No. 08/892,403) remains unavailable. In order to expedite consideration of the references, applicant may wish to resubmit the references. Any inconvenience is regretted.

#### ***Double Patenting***

3. The provisional rejection of claim 131 under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 23, 24, and 62 of copending Application No. 09/291,894 is maintained. Applicant's request to defer response to this rejection until the conflicting claims in one of the subject cases is allowed is acknowledged.

#### ***Claim Objections***

4. The objection to claim 120 under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim is withdrawn pursuant to applicant's amendment thereof.

***Claim Rejections - 35 USC § 112***

5. The rejection of claims 128-131 under 35 U.S.C. 112, first paragraph, is maintained. Applicant's arguments have been fully considered but they are not persuasive for the following reasons.

Applicant's argument that the standard for efficacy of a human vaccine does not require prevention of all subsequent infections by all possible variants of a pathogen in all human populations is noted; however, as was set forth in the previous Office action, the art teaches that live attenuated RSV vaccines have failed because they are in general not protective against subsequent infections. The art teaches that lack of protection is the general rule, not the exception to the rule. In fact, Murphy et al. (Virus Research 32:13-36, 1992, of record) teaches that to date, no successful vaccines for RSV have been developed due to a plurality of obstacles that as of yet have not been overcome (see the entire document and especially page 14, first full paragraph, through page 15, second full paragraph, and page 22, last partial paragraph, through page 26, first paragraph).

Applicant further argues that Murphy et al. do not forecast that development of a live-attenuated RSV vaccine would be attended by undue experimentation. However, the teachings of Murphy et al. are replete with obstacles that must be overcome before a successfully protective live attenuated vaccine can be developed. In fact, Murphy et al. teach "successful immunization against each of these pathogens should be achieved within this decade" (last sentence of the abstract). Absent some evidence to the contrary, a decade of experimentation in the absence of sufficient guidance from applicant's disclosure as to how the obstacles outlined by Murphy et al. can be overcome would be considered to be undue experimentation.

Regarding the value of the murine model as predictive of the efficacy of the RSV vaccine in humans, applicant argues that the "murine model data need not be precisely reflective of the activity of a recombinant RSV vaccine candidate in humans...", but must "merely be reasonably correlative to treatment in other mammals ... based on the state of the art". However, the teachings of the art do not support a reasonable correlation between the murine model and efficacy in humans. In fact, Murphy et al. teach that "it is relatively easy to protect rodents and monkeys which are only semi-permissive for RSV infection, but it is more difficult to protect the seronegative chimpanzee, a fully permissive host (see the

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sentence bridging pages 23-24). The literature references provided by applicant fail to teach away from a lack of a reasonable correlation. Rather the references teach that rodent studies are useful only as an initial screen for identifying potentially attenuated strains of RSV and that studies of protective efficacy of candidate vaccine strains must be conducted in chimpanzees. While applicant's argument that Murphy et al. describes validation testing for vaccine candidates in mice followed by chimpanzees is noted, applicant's specification does not disclose such validation testing in chimpanzees. Applicant's specification only discloses the rodent screening model. While applicant's arguments that the "art clearly accepts chimpanzees as closely faithful model subjects to humans with respect to their permissiveness and responses to RSV infections is noted, once again, it is the correlative value of the murine model in applicant's disclosure that the art teaches is unpredictable. Applicant's specification contains no disclosure or guidance whatsoever regarding administration of the claimed vaccine composition to chimpanzees. Applicant's specification only discloses data generated from a murine model, which the art teaches is not correlative with protective immunity in humans.

6. The rejection of claim 121 under 35 U.S.C. 112, second paragraph, is withdrawn pursuant to applicant's arguments, which were persuasive.

***Claim Rejections - 35 USC § 103***

7. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

The rejection of claims 63-67, 89, 93-95, 120, 121, 128, 131-136, 148, and 150 under 35 U.S.C. 103(a) as being unpatentable over Collins et al.; the rejection of claims 122, 129, and 130 under 35 U.S.C. 103(a) as being unpatentable over Collins et al. in view of Randolph et al.; and the rejection of Claim 160 under 35 U.S.C. 103(a) as being unpatentable over Collins et al. in view of Klein et al. are all maintained. Applicant's arguments have been fully considered but they are not persuasive.

Applicant argues that Collins et al. do not forecast a reasonable expectation of success for introducing significant genetic changes to yield live attenuated vaccine candidates and that Collins et al.

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do not provide specific guidance to raise the disclosure beyond what the courts have characterized as an invitation to experiment. Applicant is reminded, however, that the instant claims are not drawn to an attenuated vaccine composition. They are drawn to a recombinant virus comprising an SH gene deletion. Collins et al. is fully enabling for making such a virus as a potential vaccine candidate (see page 11566, the paragraph bridging columns 1 and 2, for example). There is no requirement that the recombinant virus taught by Collins et al. be a successful vaccine strain which elicits protective immunity because the claims are not drawn to a vaccine for eliciting protective immunity. Regarding applicant's "broad laundry list" argument, Collins et al. disclose ablating the genes for one of five specific proteins, among them the SH gene. Absent some evidence to the contrary, this points directly to making a recombinant RSV with an SH gene deletion.

#### ***NEW GROUNDS OF REJECTION***

##### ***Claim Rejections - 35 USC § 112***

8. Claim 120 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Applicant has amended claim 120 to recite a complete virus. Claim 120 depends from claim 63, which recites that the virus has a partial or complete gene deletion, and thus would be considered to be "incomplete". It is unclear how a virus with part of the genome deleted can be viewed as a complete virus. Clarification and correction are required.

#### ***Conclusion***

9. No claims are allowed.

10. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

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A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Brenda Brumback whose telephone number is (703) 306-3220. If the examiner can not be reached, inquiries can be directed to Supervisory Patent Examiner Anthony Caputa whose telephone number is (703) 308-3995. Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (703) 308-0196. Papers related to this application may be submitted to Group 1600 by facsimile transmission. Papers should be faxed to Examiner Brenda Brumback, Art Unit 1642 and should be marked "OFFICIAL" for entry into prosecution history or "DRAFT" for consideration by the examiner without entry. The Official FAX telephone number is (703) 872-9306 and the After Final FAX telephone number is (703) 872-9307. FAX machines will be available to receive transmissions 24 hours a day. In compliance with 1096 OG 30, the filing date accorded to each OFFICIAL fax transmission will be determined by the FAX machine's stamped date found on the last page of the transmission, unless that date is a Saturday, Sunday or Federal Holiday with the District of Columbia, in which case the OFFICIAL date of receipt will be the next business day.

  
Brenda Brumback  
Patent Examiner